(54) Title: ERYTHROSEDIMENTATION RATE (ESR) TEST APPARATUS

(57) Abstract

ESR measurement apparatus comprising a plurality of light sources (13) illuminating the blood sample contained inside a suitable test-tube (16), the light transmitted being received by a plurality of photoreceivers (15). The signals received by the photoreceivers are continuously processed by a microprocessor unit (11) to determine the instantaneous position of the erythrosedimentation level and consequently its displacement rate.

ERYTHROSEDIMENTATION RATE (ESR) TEST APPARATUS

Field of the invention

The present invention refers to a ESR test apparatus. The test is performed with a blood sample quantity and a measurement time considerably reduced in respect

5   of the traditional ones. The use of small blood quantities and of a quick measuring method results in particular advantages when emergency applications are required.

Background of the art

In the medical analysis field it is known since a long time that the erytrocites of the

10   blood of people affected by some diseases, particularly inflammatory diseases (for example: rheumatism) present an higher sedimentation rate. The erytrosedimentation rate test is utilized to control the cortisone therapy of rheumatical diseases. The ESR increase is substantially due to some changes in the blood plasma and in the erytrocites, which facilitate the formation of erytrocites

15   agglomerates, also called "rouleaux".

In practice, it is generally used the traditional method of A. Westergreen, dated 1921, in which the venous blood is mixed with an anticoagulant agent (for example trisodium citrate in a range of 0,1-0,11 moles/l, or EDTA). According to this method, a pipette (30 cm long and graduated from 0 to 200 millimeters) is

20   filled by suction up to the 0 mark and then it is vertically placed on a suitable pipette holder. After 60 minutes at room temperature, a first reading of the erytrosedimentation level is performed: the distance, on millimeters, between the plasmatic meniscus and the erytrosedimentation level delimiting the thicker and duller portion represents the ESR value. After one hour it is possible to perform a

25   second reading. A further well known method is the Wintrobe method, employing

a probe-tube of hematocrit. Also in this case the results are expressed in mm/h.

It is also known that by tilting the pipette of 45° the ESR considerably increases and, in turn, the time requested for the test decreases.

US patent No. 4 801 428 (Homolko et al.) in the name of "Becton, Dickinson and Company", describes a kit for measuring simultaneously the ESR of the erytrocites contained in several test-tubes.

The kit consists of a main trasparent body inside which several cavities are provided. Each cavity can house a test-tube for ESR test. Before introducing the test-tube, a cylindrical graduated sleeve having at least a flat portion on the lateral surface has to be introduced into the cavity. Obviously, the sleeve presents transversal dimensions intermediate between the test-tube and the cavity dimensions. The operator can vertically displace the sleeve using a transversal rubber-coated pin, frictionally engaged with the flat portion of the lateral surface of the sleeve. Due to the transparency of the body inside which the cavities are placed, moving the sleeve the operator can fix the "0" mark of the graduated scale with the superior blood meniscus level at the starting time of the test. After one hour, the operator can appreciate on the same graduated scale of the sleeve how much the erytrocites meniscus has lowered. The Italian Patent No. 1,192,490 (in the name of Diesse Diagnostica Senese S.r.l.) refers to an ESR test apparatus operating on several samples and comprising: a test-tube holder equipment, able to rotate around an horizontal axis; time control means to move/fix the equipment with the test-tubes in vertical position; and a structure vertically movable in respect of the test-tubes, the structure being provided with photometric sensor means and with information which are related to each test-tube. The apparatus claimed in the Italian Patent allows to use dimensionally reduced test-tubes and subsequently to

correlate the results obtained with such test-tubes with the standard values of the traditional 30 cm long pipette of the Westergreen method. This solution is an improvement of the apparatuses described in other documents, but presents some drawbacks substantially consisting in that, to perform the erytrosedimentation level reading, it requires a movable structure carrying the photometric sensor means. It results in complicated displacement devices, which make impossible to obtain an high resolution of the sedimentation level reading, and also involves too long reading times, which are disadvantageous in case of emergency applications. Furthermore, due to the particular reading system adopted, it is necessary to "follow" by photometric sensor means the displacements of the erytrosedimentation level. As a further drawback, the apparatus has an unique and prefixed threshold acceptability value of the light quantity received by the sensors which, in presence of some kind of samples, could introduce errors. It is to be noted that the quality and the accuracy of the reading resolution are essential in order to properly correlate the readings obtained with as small as possible test-tubes with the standard reference values of Westergreen. On the other hand, it is evident that the reading resolution has to be the highest possible in order to reduce the test-tube dimensions and the quantity of blood sample required. US patent No. 4 848 900 (Kuo et al.) also describes a system in which a light beam "follows" the erytrocites level, in combination with a photometric sensor which allows to measure the sedimentation level changes in a test-tube substantially of the kind used in the Westergreen method. In that patent it is also described a microcomputer and a step by step motor used to displace the sensor along the test-tube and to operate a feedback control of the system. Also in this case, the costs are relatively high and the movable elements cause an

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inaccurate reading.

Summary of the invention

The apparatus according to the invention allows to overcome said prior art drawbacks.

5   Such object has been reached by an apparatus able to read the erytrosedimentation level by a plurality of fixed photometric sensors aligned one after the other and all constituting a unique sensor assembly intended to receive the light from the analyzed test-tube. The reading system is completely at the solid state and does not require the movable mechanisms and transduction systems

10   (light sources and movable sight photocells) of the known methods. The reading sensors employed in the apparatus allow a reading resolution of 125 micron and a continuous electronic scanning of the erytrosedimentation level. The determination of the level is obtained utilizing the signals produced by the optical sensors of the reading assembly, which are placed parallel to the test-tube axis, and by a

15   subsequent numeric processing of the output of each sensor. The sedimentation level position is appreciated inside a reading range of 128 or more aligned points, the number of which depends on the kind and on the number of the choosen sensors, each of them corresponding to a level point. The brightness of each point is measured by a continuous and accurate discrimination of 256 grey levels (when

20   8 bit A/D converters are employed) inside the erytrosedimentation region, and the sedimentation level is determined.

According to a further feature of the invention, such numeric processing includes an adaptive recognition of the grey level, performed for each reading cell and which allows both to employ more or less trasparent test-tubes and to analyze

25   with the same accuracy blood samples having different trasparency.

This specific solution also allows to measure the erytrosedimentation rate of the sample in the test-tube according to two different ways:

(i) by measuring the displacement of the erytrocites level in a predetermined reading time (for example 8 min.);

5   (ii) by measuring the time that the erytrocites level requires to complete a predeterminate displacement (for example 10 mm).

In the latter case, the measurement time is proportionally reduced according to the erytrosedimentation rate. The value obtained by the numeric processing is subsequently correlated to the ESR clinical value by a suitable correlation table.

10   The apparatus generally includes a light source, constituted for example by a plurality of infrared photoemitter diodes, which illuminates the blood sample contained in a suitable test-tube. The trasmitted light is received by a photoreceiver sensors assembly which is parallel to the longitudinal axis of the test tube. The signals emitted by the photoreceiving sensors are continuously

15   processed in the described way by a microprocessor device, in order to determine the sedimentation level. The displacement rate of such level is measured according to a method (i) and/or (ii) and then correlated to standard ESR values by a suitable correlation table which is realized considering also the relevance of the room temperature measured by a suitable sensor of the apparatus.

20   It is also possible to use a linear sensor CCD (Charge Couple Device) in alternative to said photodiodes arrays.

The invention comprises a diagnostic sample test-tube allowing a quick ESR analysis with an as small as possible quantity of the blood sample contained in the test-tube and avoiding the "attachment" effect of the blood to the internal walls of

25   the test-tube. As it is known, said effet is an unsolved problem which causes a

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delay because the measurement can start only after the fall of blood red corpuscles "attached" to the walls has finished.

Said objects have been reached according to the invention with a test-tube having a prismatic hollow body and a cylindrical head of slightly bigger dimensions. The

5 external walls of the body have glazed surfaces to improve the test-tube handling and to allow to append indentification code bar labels.

Furthermore, the test-tube presents a trasparent portion intended to allow the visual inspection of the proper filling of the blood sample contained in the test-tube.

10 The test-tube can also be provided with a support ring which lifts up the test-tube when the filling is unsufficient (the blood level does not reach as required the receiving sensors quote) and the measurement would not be enabled by the microprocessor unit.

According to a further feature of the invention the test-tube is made of water-

15 repellent material in order to reduce the "attachment" effect of the blood to the internal walls during the preliminary operation of shaking of the sample and to allow the use of small blood sample quantities.

Drawings list

The invention will be better explained with reference to the following non-limitative

20 drawings, in which:

fig.1 illustrates a schematic reading cell of an apparatus according to the invention;

fig.1a shows several reading cells of fig.1 inside a preferred embodiment of the apparatus;

25 figs. 2-5 illustrate ESR diagrams; in particular figs. 4,5 illustrate ESR diagrams

obtained by reading cells employing a linear sensor CCD (Charge Couple Device);

figs. 6a,6b illustrate respectively a top view and a side view of a preferred

embodiment of the invention, where the horizontal inclination angle α is shown;

fig.7 shows the section AA of fig.6b;

5   fig.8 schematically shows the electronic equipment of the apparatus;

fig.9 shows a side view of the test-tube according to the invention;

fig.10 shows a second lateral view of the test-tube of fig.1;

fig.11 shows an enlarged sectional view according to section AA of the test-tube

of fig.2;

10   fig.12 shows a test-tube having a closing plug;

fig.13 shows a test-tube plug.

Detailed description of the invention

Fig. 1 schematically shows a reading cell of the apparatus of the invention.

According to fig.1, a microprocessor device 11 controls all the operations. In

15   particular it controls a reading cell 21, delimited in the figure by a dotted line, able

to appreciate the grey level at the different blood sample quotes and,

subsequently, to allow the erytrosedimentation level determination.

Cells 21 present driving means 12 of photoemitter diodes 13 and means 14 to

amplify, digitally convert and transmit the analogic signals received from fixed optical

20   reading sensors 15, placed at the opposite sides of the test-tube in respect of said

photoemitters 13.

With reference to figs. 6a, 6b, 7 a preferred embodiment of an apparatus 10 is described,

which works with a plurality of samples.The apparatus is able to independently

measure the ESR of the different blood samples contained in the test-tubes and

25   which can be simultaneously analyzed. The apparatus comprises several reading

pockets 23, each of them is provided with a reading cell. The pockets share the driving device 12 and the means 14 to amplify, convert and transmit the reading signals. In particular, in the drawings are shown several test-tubes (sixteen test-tubes), placed inside an equal number of pockets 23 realized inside a base 24.

5 The base 24 preferably rests on an orizzontal plane Z (in figure 6b plane Z is counter-clockwise rotated of an angle α to better show the drawing), so that the pockets and the test-tubes have an inclination α, for example 25°, in order to reduce the required sedimentation time.

As fig.7 shows, and according to fig.1, each test-tube 16 is placed between

10 photoemitter diodes 13, preferably infrared emitters, and photoreceiver sensors 15. The test-tube is made of trasparent or translucent material and has two glazed lateral portions usefull to handle the test-tube, or to write words (name and number of the patient) for example by pen, or to append labels with bar codes to be read by the optical pen 22 of fig.8 to identify the patient corresponding to each

15 test-tube. A suitable portion, or window 26, defines the lower limit of the proper filling of the test-tube. Below such limit the apparatus does not perform the measurement.

Horizontal curtain filters 27 are used to reduce the action on the sensors of the slanting light beams and consequently increase the resolution capability of the

20 receiving sensors. The apparatus includes a keyboard 28, a digital display 29 and a printer 30, of the known type.

In the use, the test-tubes 16 containing the blood sample are shaked to break possible "rouleaux"; this operation is done manually or automatically by a suitable external shaker if the analysis is not immediately subsequent the blood sample.

25 After shaking, each test-tube 16 is placed inside the reading pocket, so that the

corresponding reading sensors can verify its presence and communicate it to the microprocessor unit device.

By means of a couple of sensors of assembly 15 placed at the window level, the microprocessor unit verifies that the blood level in the test-tube is above said

5   window limit and abilitates the reading operation. Otherwise, it is reported that the measurement is impossible or that a support ring 37 is required for that test-tube. The spatial limits of the reading range can preferably vary between 16 and 70 mm depending on the kind and on the number of the sensors employed, while the quote reading resolution is preferably of 125 micron, depending only on the

10   specific technology of the reading sensors.

The scanning is repeated with a time period of 250 milliseconds for an average test time (starting from time "0") of approximately 8-10 min., depending on the specific dynamic to be observed.

Referring to fig.1a, the reading sensors 15 of the apparatus 10 have a common

15   clock signal input 9. Each reading sensor 15 of the reading cells is constituted by a plurality of superimposed and aligned photoreceiver diodes which receive the light transmitted by the illuminated sample and produce analogic signals. Each signal corresponds to the grey level of the sample quote at which the sensor is positioned. After each scanning the analogic signals are amplified, digitally

20   converted by a D/A converter, and transmitted to the unit 11 by a common device 14. After the signal convertion, the software implemented in the microprocessor unit 11 measures continuously and with accuracy the light received by the different aligned diodes of each reading cell. The values measured are utilized to determine the erytrosedimentation level in the test-tubes. For example, such level

25   is determined associating it to brightness variation of a predetermined intensity of

the light received by two or more adjacent diodes.

Advantageously, this solution does not require the definition of a reference threshold value of light and shade, which always introduces a wide margin of error.

5   It is also provided an adaptive recognition signal processing which makes the correct reading of each cell independent from the optical characteristics of the test-tube and of the blood samples.

The processing can consist, for example, in the determination of a brightness variation value, which the sedimentation quote level of each test-tube is

10   associated to.

Advantageously, the continuous scanning and the reading self-adjustment allows to employ test-tubes made of water-repellent material, for example polypropylene, which are cheap and suitable to the specific test to be performed because they present a reduced "attaching" effect to the test-tube walls after the initial shaking.

15   Such materials have never been used in the automatic apparatuses because their opacity involves too wide margins of error in the light/shade threshold recognition when in presence of a non-continuous digital (0/1) reading of the grey level.

With reference to fig.8, it is schematically shown the electronic equipment of the apparatus, comprising a microprocessor unit 11 connected to the following

20   components: a bar code reader 22 constituted for example by an optical pen; two groups each comprising eight receiving sensors assemblies 15 associated to an equal number of reading pockets. The pockets are provided with lighting bicoloured red/green LED controlled by the unit 11 and used to notify to the user when each test is finished; an assembly of sixteen photoemitters 13 and a room

25   temperature sensor 34; a printer 30; a keyboard 28; a display 29; a supply line 32

and serial line 33 for possible connection to an external computer.

In the figure it is also shown the linkage to a connector 31 for microchip cards. Advantageously, according to the invention, the apparatus is able to flexibly perform several functions on the basis of specific data encoded on a microchip

5   card and processed by the unit 11. For example, it is possible to use the card as a validation key of the apparatus; to associate a group of patients to a specific measurement test; to verify the number of the tests performed or of the test-tubes utilized; to update as required the functional parameters of the apparatus.

A still further characteristic of the invention is the possibility to modularly expand

10   the apparatus by external lines 36 and connecting the electronic equipment of an apparatus acting as "master" to one or more peripherical "sleeve" apparatuses assembled without keyboard, display and printer, and which send to the master apparatus the data of the tests performed.

With reference to the annexed diagrams, figure 2 shows in abscissa the reading

15   time expressed in minutes and, in ordinate, the erytrocites level position.

From the diagram it is clear that the sedimentation process has a roughly linear behaviour starting after a first step in which the observed phenomenon is influenced by the red blood corpuscles turbolence due to the initial shaking. After a first period (approximately 2-3 minutes) during which the phenomenon can have

20   an opposite dynamic (raising of the sedimentation level) due to the red blood corpuscles which fall from the internal walls of the test-tube, the erytrocites level has an appromixately linear lowering.

The initial raising effect can be considerably reduced by a suitable choice of the test-tube shape and material. However, the apparatus can appreciate the dynamic

25   of that particular process, because it continuously controls the phenomenon and

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abilitates the zero point reading and the erytrosedimentation rate measurement only when the increasing of the stops and the diagram behaviour becomes monotone.

As already said, the apparatus functioning is based on the measurement of the

5   erytrosedimentation level lowering rate in a predetermined time or distance, and on a subsequent correlation of such data with clinical reference values. For example, measuring the time required for a 5 mm displacement of the sedimentation level, it is possible to obtain a rate value to be correlated to the clinical parameter.

10   In order to assure a still better accuracy the apparatus 10 can be connected to a room temperature sensor 34 to adjust the measurements which are influenced by the room temperature.

Further possible improvements of the measurement are the following:

(A) tilting of the test-tube (angle α of fig.6b) in respect of the vertical position, in

15   order to increase the sedimentation rate; such increasing allows to reduce the required time for the clinical parameter determination because it is possible to correlate the "tilted test-tube" value with the reference one;

(B) the system can be provided with an external shaking device to automatically shake the blood samples;

20   (C) infrared transparent curtain filters can be adopted on the receiving sensors, and possibly on light sources, to increase the protection against the external light.

In Fig.3, the ordinate value expressed as "digit" corresponds to the sensor resolution, in the present case 125 micron. The figure shows only the linearized

25   behaviour of the diagrams of figure 2, between approximately 3 and 6 minutes, for

various ESR values.

In the figures 4 and 5 there is shown a pencil of subsequent scannings, for each of them the quote position is on the abscissa axis and the received light quantity is on the ordinate axis. In the case of figure 4, the sedimentation level, which can be appreciated by the brightness variation measured by the diodes corresponding to that level, has a displacement from point B1 to A1 (on 6 minutes) and the segment length, after correlation with a suitable correlation table, corresponds to a value ESR=15.

In figure 5 the erytrosedimentation level has a displacement (in a time period of 6 minutes) from B2 to A2, which ESR=85 corresponds to. With reference to figures 9-13, a test-tube according to the invention is constituted by an elongated prismatic hollow body 100, on which a cylindrical hollow head 200 is superimposed. In the described embodiment, the front and rear walls 120 of the body 100 have slightly bigger dimensions than the lateral walls 110 and present a glazed portion, represented in figure 9 by hatching, which has a polished zone, or window 130, in the upper part of body 100. The lateral walls 110 are trasparent to allow the light passage and one of them presents a reference mark 190 impressed on the upper part. The body 100 presents a slightly conical external outline, while the internal cavity has a constant section.

The head 200 presents a cavity constituted by a cylindrical part 140 for the insertion of a closing plug 170 and a lower part 150 which remains available to facilitate the shaking of the sample contained in the test-tube.

According to the invention, the test-tube contains an anticoaugulant product and is made of water-repellent material, preferably PET ®, polypropylene, polyethylene or nylon for food applications. With this solution, even if the internal cavity is

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extremely small, the "attachment" effect of the blood to the internal walls is reduced and does not delay the sedimentation dynamic.

Preferred dimensions of the body 100 are: length approximately 45 mm; internal cavity section 4X6 mm.

5   Advantageously, the very small dimensions of the test-tube are useful to be used in the described apparatus performing many simultaneous tests. At the same time, the test-tube is particularly advantageous to be used with the described light sources and photometric sensors placed at the opposite sides of the test-tubes. The sensors are placed along a measurement window (in the described test-tube

10   it is a portion of the side walls 110) having dimensions correlated to the sensors dimensions (a few mm of length) and which have to be as small as possible to reduce the required blood quantity of each sample. The front and rear walls 120 have a bigger width in order to extend the optical path of the light through the sample and to improve the measurement reliability with a determined blood

15   quantity.

With reference to figures 12,13, a closing plug 170 is shown, which is inserted inside the cavity 140 of the head 200 to leave an available free space sufficient to allow the sample shaking. Plug 170 presents a lateral groove 180 through which vacuum can be created before closing the test-tube. Advantageously, the vacuum

20   allows to fill a suitable dose of blood from a butterfly shaped sampling valve, without opening the plug and to avoid any risk for the user to touch the contained blood.

Without outgoing from the invention scope it is possible to the man skilled in the art to modify the ESR apparatus of the present description with all the

25   improvements and modifications suggested by the general experience and the

technical progress.

CLAIMS

1. ESR test apparatus, characterized in that it comprises at least one reading cell comprising at least one light source (13) able to illuminate a blood sample contained inside a suitable test-tube (16), the light trasmitted through the sample being received by at least a fixed photoreceiver assembly (15) of the cell which extends parallel to the test-tube and is placed at its opposite side in respect of the light source; and in that and the output signals of the photoreceiver are obtained by repeated high resolution scannings which are performed along the test-tube by said photoreceiver assembly and are continuously processed by a microprocessor unit (11).

2. Apparatus according to claim 1, characterized in that said photoreceiver assembly (15) is constituted by a plurality of superimposed photodiodes aligned along the test-tube, and that said light source (13) is constituted by a plurality of photoemitter diodes.

3. Apparatus according to the preceding claims, characterized in that the reading range extension of said assembly (15) can vary between 16 and 70 mm, having a reading resolution of 125 micron.

4. Apparatus according to the preceding claims, characterized in that for each scanning, preferably repeated with a time period of 250 milliseconds, said unit (11) continuously processes the signals from the assembly (15), determining the instantaneous position of the erytrosedimentation level of the blood sample in order to determine its displacement rate and the ESR of the analyzed sample by correlating such rate with suitable correlation tables.

5. Apparatus according to the preceding claims, wherein the displacement rate of the erytrosedimentation level is calculated measuring the displacement of said

3 quote in a predetermined time.

1 6. Apparatus according to the preceding claims, wherein the displacement rate of

2 the erytrosedimentation quote is calculated measuring the time required to have

3 a predetermined displacement of said quote.

1 7. Apparatus according to claim 1, wherein said photoreceiver assembly (15) is a

2 linear sensor CCD (Charge Couple Device).

1 8. Apparatus according to claim 1, wherein said microprocessor unit (11) is

2 connected to a microchip card reading device (31).

1 9. Apparatus according to claim 1, wherein said microprocessor unit is connected

2 to a room temperature sensor (34).

1 10. Apparatus according to the preceding claims, characterized in that it presents

2 a plurality of reading pockets, preferably sixteen, each of them provided with an

3 autonomous reading cell to independently measure the ESR of samples

4 contained in all or part of the test-tubes.

1 11. Apparatus according to the preceding claims, characterized in that said

2 pockets are realized inside a base (24) and are tilted of an angle (α), preferably

3 25° in respect of a vertical axis.

1 12. Apparatus according to the preceding claims, characterized in that each

2 reading pocket is provided with a LED, preferably a bicoloured red/green LED,

3 which notifies if a measurement is being performed.

1 13. Apparatus according to the preceding claims, characterized in that it provides

2 infrared transparent filters for the photoreceivers and/or for the light sources, in

3 order to improve the insulation from the external light.

1 14. Apparatus according to the preceding claims, characterized in that it provides

2 horizontal curtain filters to reduce the influence of the obliquous light beams.

1 15. Apparatus according to the preceding claims, characterized in that it has

2 external lines (36) to connect one or more peripherical apparatuses, possibly

3 without printer, display and keyboard.

1 16. Apparatus according to the preceding claims, characterized in that said

2 microprocessor unit (11) is connected to a code bar reader (22) preferably an

3 optical pen.

1 17. Apparatus according to the preceding claims, characterized in that said unit

2 (11) operates an adaptive recognition of the light/shade level of each sample.

1 18. ESR sample test-tube, particularly for ESR tests, characterized in that it is

2 constituted by an elongated prismatic hollow body (100), on which a cylindrical

3 hollow head (200) is superimposed; the front and the rear walls (120) of the

4 body (100) are wider than the side walls (110) and present a glazed surface

5 with a polished window (130) intended to visual inspection of the sample, while

6 the side walls (110) are trasparent to allow the light passage.

1 19. Test-tube according to claim 18, characterized in that the body (100) extends

2 for approximately 45 mm having a slightly conical external outline and the

3 internal cavity has a constant section of preferably 4X6 mm.

1 20. Test-tube according to claim 18, characterized in that said head (200)

2 presents a cavity constituted by a cylindrical part (140) to house a closing plug

3 (170) and a lower part (150) which is available to allow a proper shaking of the

4 blood sample of the test-tube.

1 21. Test-tube according to claim 18, characterized in that it is made of water-

2 repellent material, transparent to the measuring light radiation.

1 22. Test-tube according to claim 18, characterized in that it is provided with a

2 rubber closing plug (170) to be sealingly introduced into the cavity (140) of the

3   head (200) and having a lateral groove (180) to create a vacuum inside the

4   test-tube when the latter is closed.

1   23. Test-tube according to claim 18, characterized in that it is provided with a
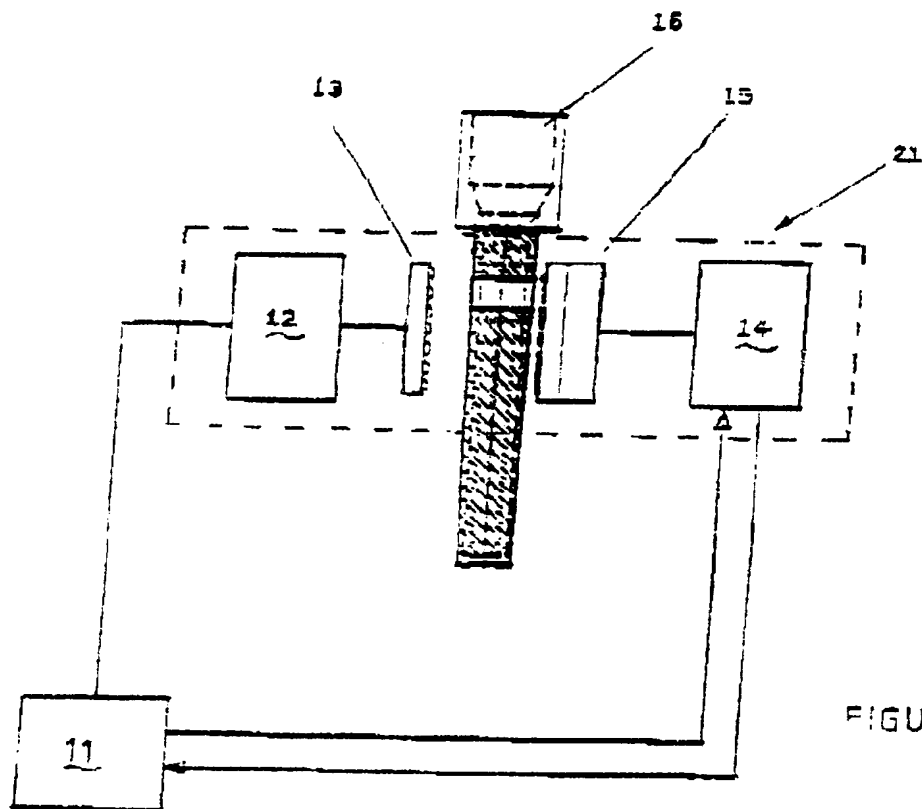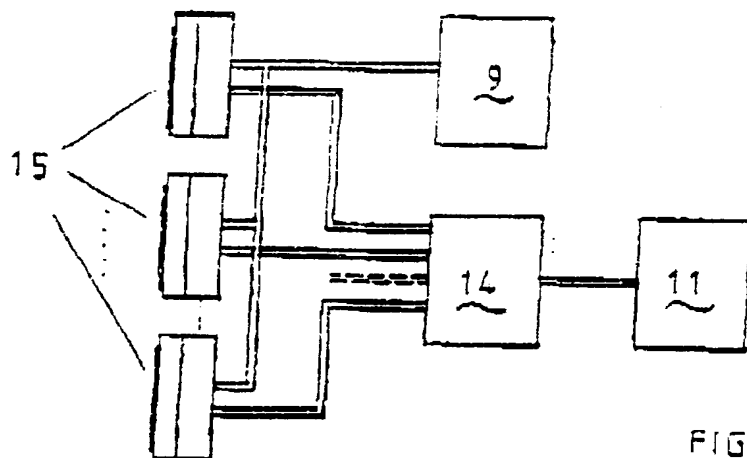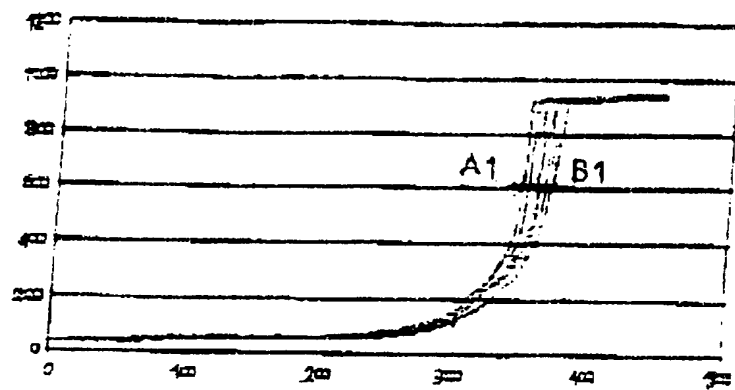
2   support ring (37) of a predetermined height.
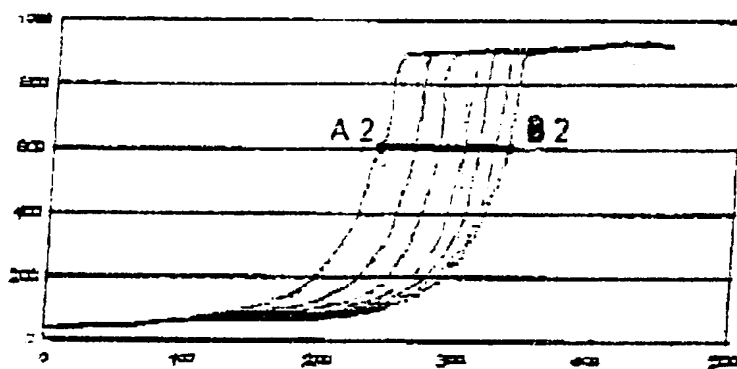
FIGURE 1

FIGURE 1a

FIGURE 4

FIGURE 5

FIGURE 2

FIGURE 3

FIGURE 6b

FIGURE 6a

Sec. A-A

FIGURE 7

FIGURE 8

FIG.11

Se. A-A
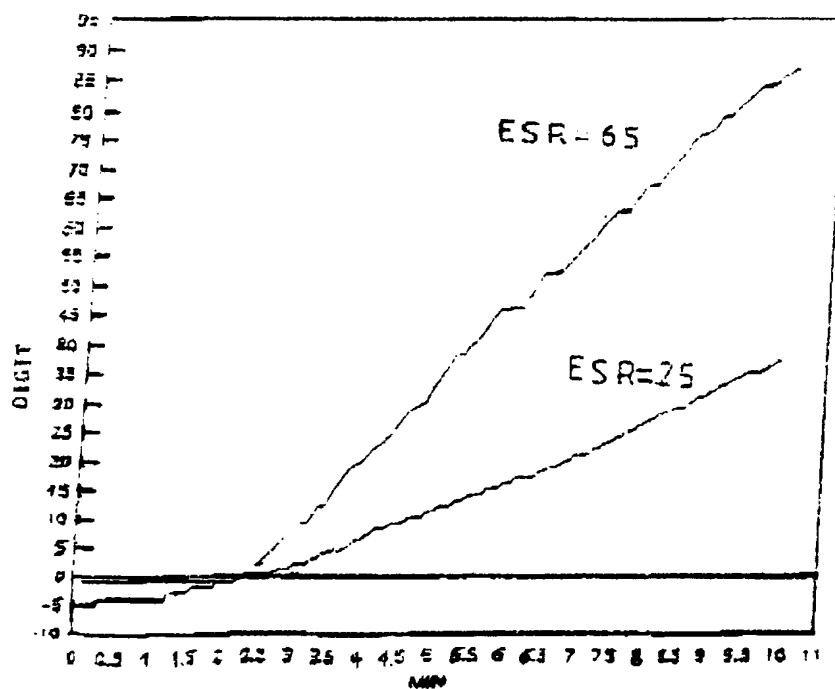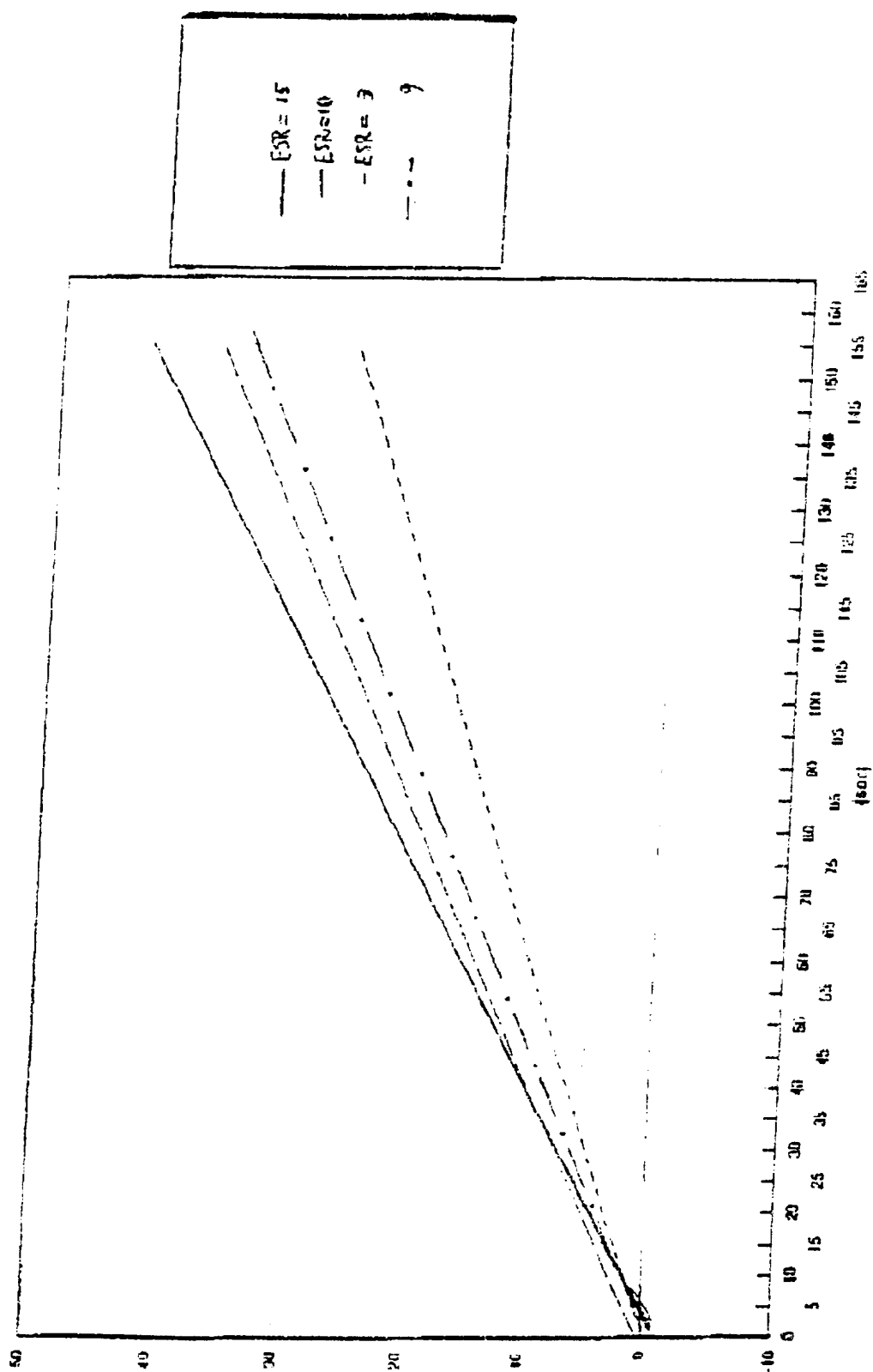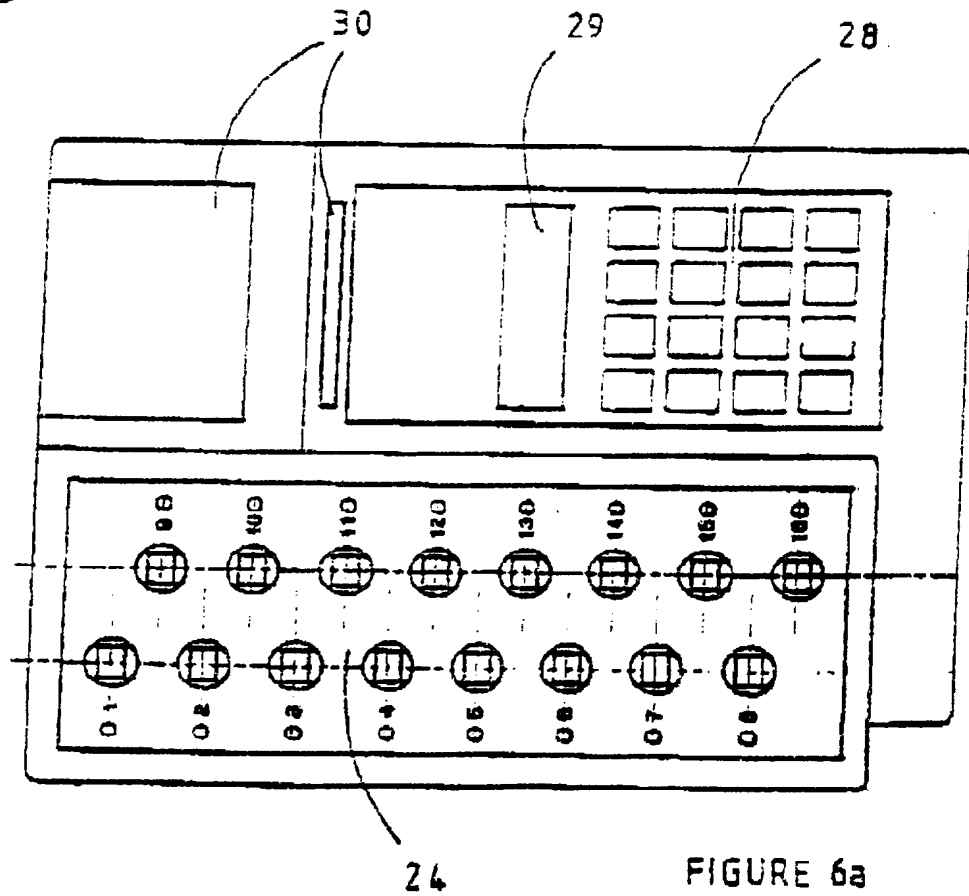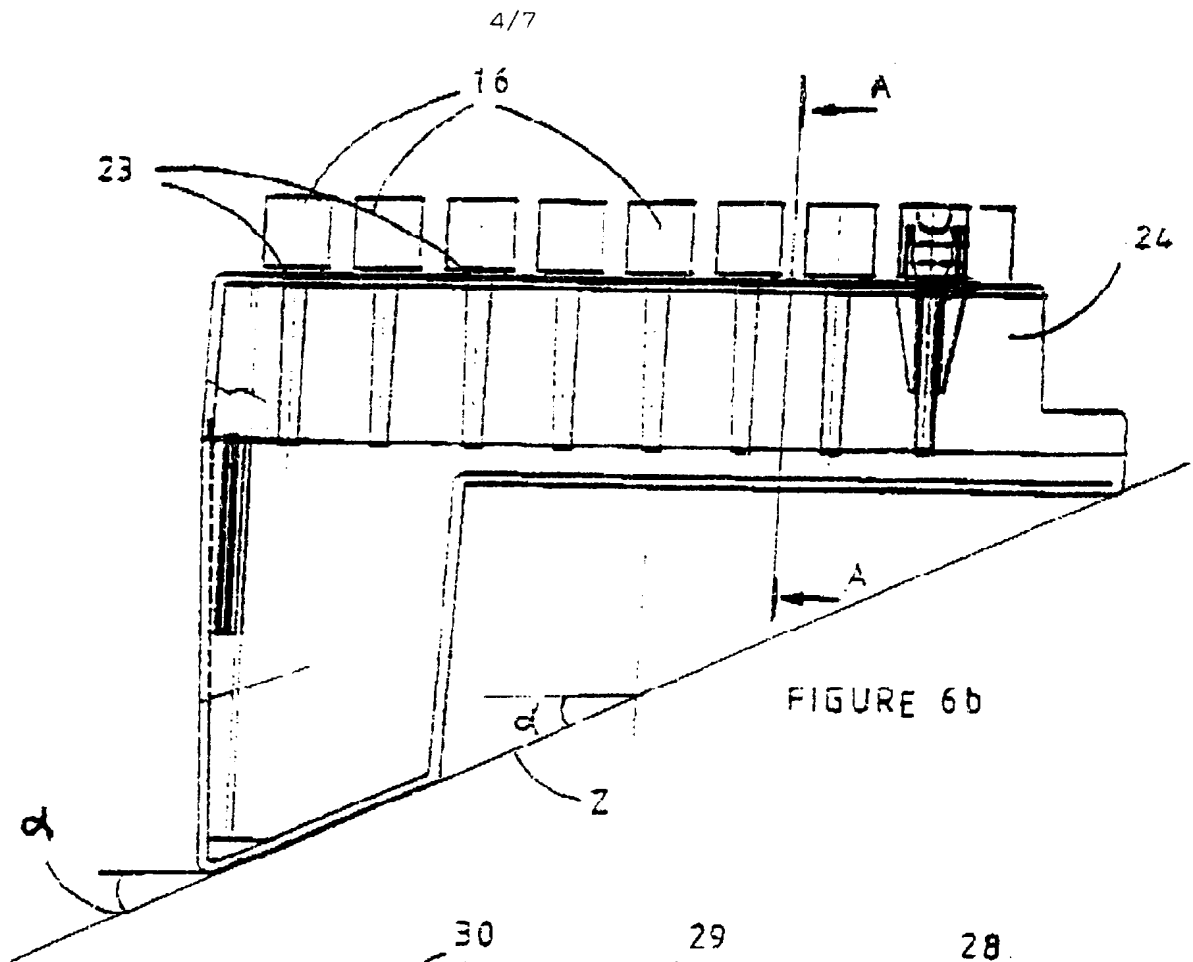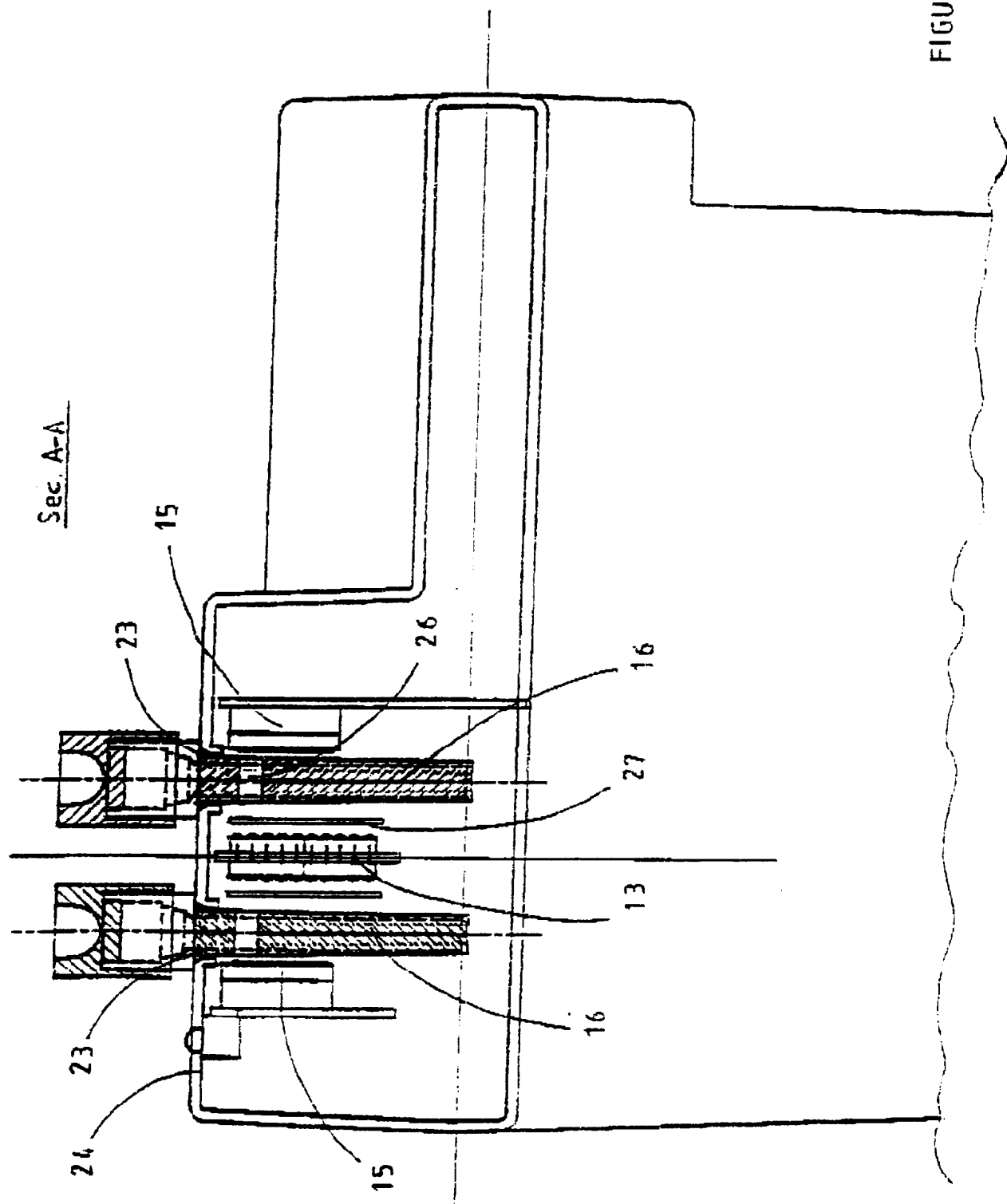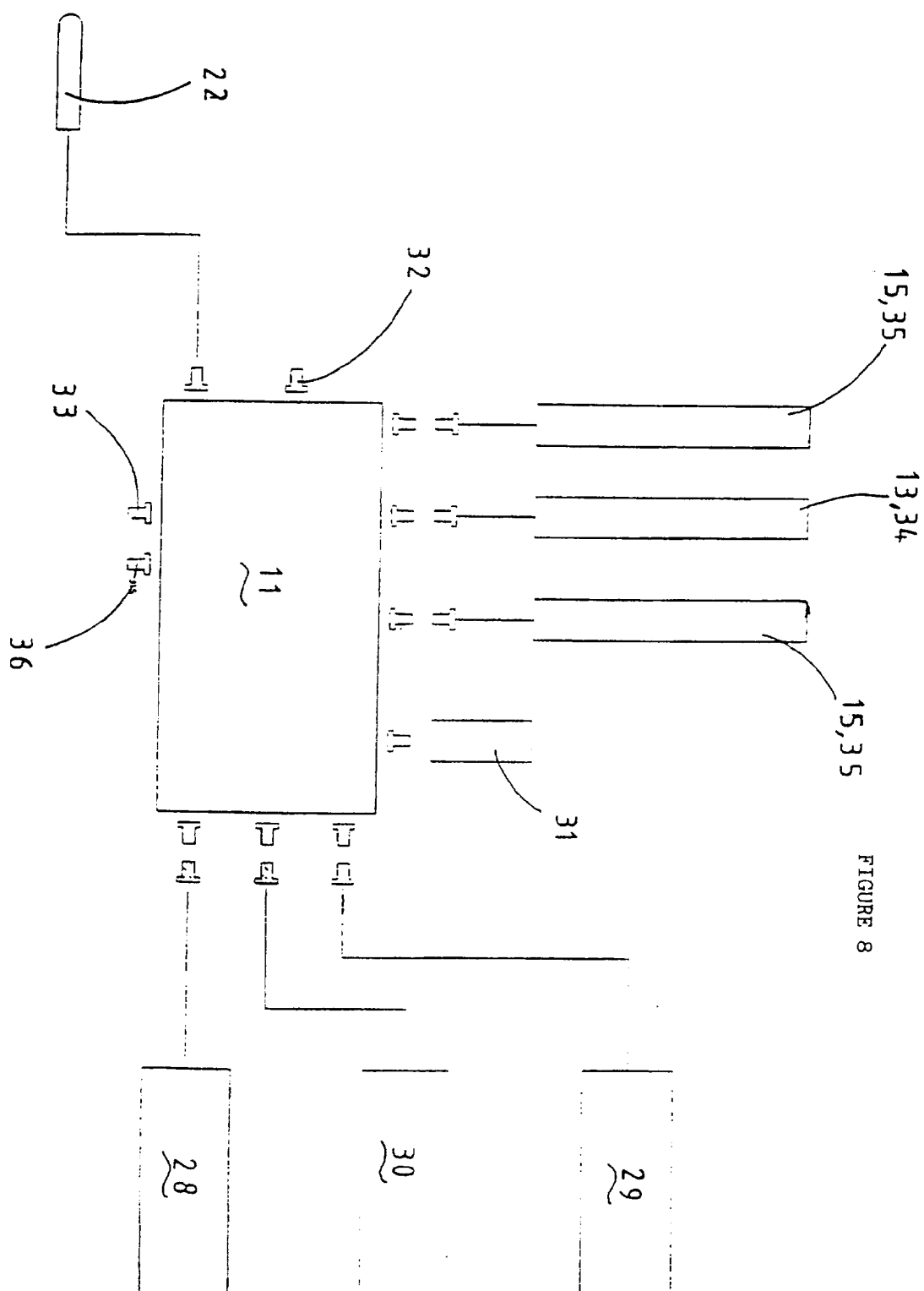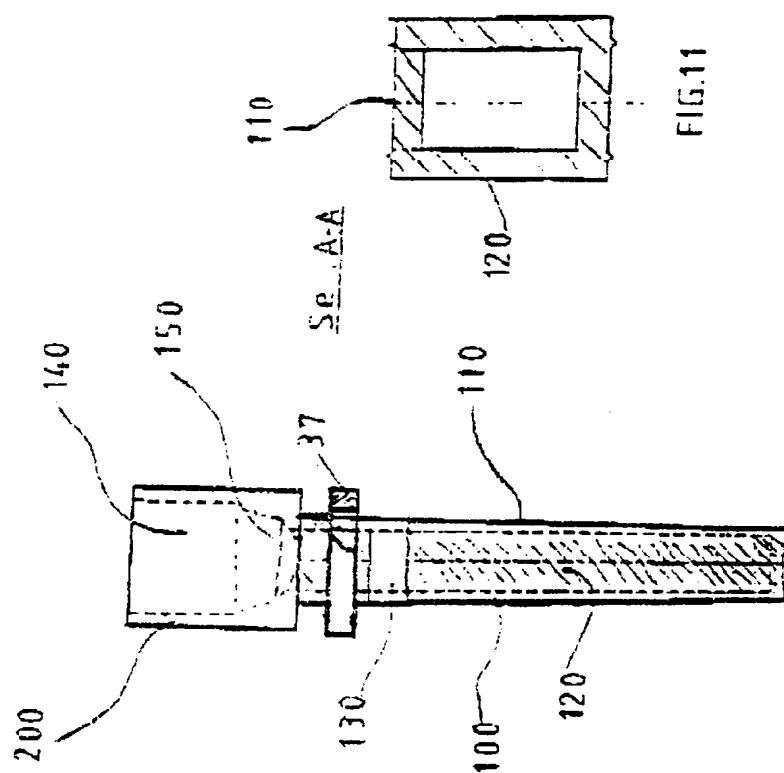
FIG.9
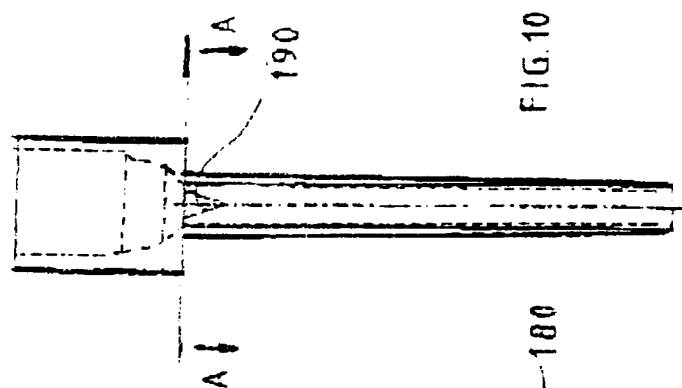
FIG.10
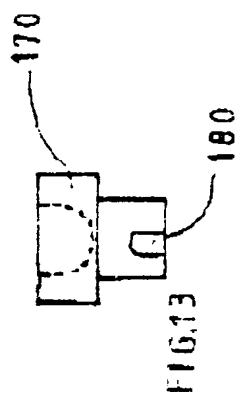
FIG.13

FIG.12

INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6   G01N15/05

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6   G01N   B01L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 342 730 A (SCHOUTEN THEODORUS) 23 November 1989 see the whole document	1,7,9, 15,16
Y		10-12
Y	FR 2 652 416 A (DIESSE DIAGNOSTICA SENESE SRL) 29 March 1991 see claim 1; figures 1,2	10-12
X	DE 92 16 127 U (ORTH HELMUT PROF DR) 7 April 1994 see page 4, line 18 - line 35; claim 1	1,7
X	US 5 003 488 A (HARDY FRANCOIS) 26 March 1991 see column 4, line 19 - line 35	1,7

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[X] Further documents are listed in the continuation of box C.   [X] Patent family members are listed in annex.

° Special categories of cited documents :

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Date of the actual completion of the international search	Date of mailing of the international search report
11 November 1997	10.12.97

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Brison, O

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
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X	US 4 710 874 A (CINQUALBRE PAUL-HENRI) 1 December 1987 see column 3, line 23 - column 4, line 55 ---	1,7
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A	US 4 392 497 A (GHAUSSY RAHMAT U) 12 July 1983 see column 2, line 9 - line 26; figure 2 -----	18,23

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